Chapter 8
Lipids and Proteins Are Associated in Biological Membranes

SUMMARY

Section 8.1

- Lipids are compounds that consist mostly of nonpolar groups. They have limited solubility in water, but dissolve freely in organic solvents.

Section 8.2

- Lipids are frequently open-chain compounds with a polar head group and a long nonpolar tail.
- Glycerol, fatty acids, and phosphoric acid are frequently obtained as degradation products of lipids.
- Another class of lipids consists of fused-ring compounds called steroids.

Section 8.3

- Lipid bilayers are large assemblies of molecules. The polar head groups of the lipid molecules are in contact with an aqueous environment. The nonpolar tails of the lipids are out of contact with the aqueous environment. The bilayer is like a sandwich with polar head groups as the bread and the nonpolar tails as the filling.
- Bulkier molecules tend to be found in the outer layer, rather than in the inner one.
- The presence of saturated fatty acids and of cholesterol tends to stiffen the bilayer.
- The packing of molecules in the bilayer can undergo a reversible transition from order to disorder.

Section 8.4

- Proteins combine with lipid bilayers to form membranes.
- Peripheral proteins are loosely attached to one surface of the membrane by hydrogen bonds or electrostatic attractions.
- Integral proteins are embedded more solidly in the membrane and, in some cases, may be covalently attached to lipid anchors.

Section 8.5

- The fluid-mosaic model is the most usual description of membrane structure. In this model, the proteins “float” in the lipid bilayer without extensive interaction between the two.

Section 8.6

- There are several ways in which molecules are transported across cell membranes, and proteins play a role in most of them.
- In simple diffusion, small, uncharged molecules cross the membrane without a carrier protein. In facilitated diffusion, substances bind to a carrier protein. Neither process requires energy, and the two together are called passive transport.
- In active transport, energy is required, either directly or indirectly. Large membrane proteins play a key role in the process.
- Proteins serve as receptors for substances that bind to cell surfaces.

Section 8.7

- The structures of the lipid-soluble vitamins—A, D, E, and K—are ultimately derived from five-carbon isoprene units, which also play a role in lipid biosynthesis.
- Vitamin A plays a critical role in vision. Vitamin D is necessary for bone integrity because of its role in calcium and phosphorous metabolism. Vitamin E is an important antioxidant, and vitamin K plays a role in blood clotting.

Section 8.8

- Prostaglandins are compounds of related structures derived from long-chain fatty acids. They have a number of physiological roles, including control of smooth muscle contraction, development of inflammation, and inhibition of platelet aggregation. The last of these three roles makes them objects of research on ways to prevent heart disease.
- Leukotrienes are also derived from fatty acids. They play a role in smooth muscle contraction in the lungs. Drugs that block the binding of leukotrienes to their receptors in lung tissue are under study for the treatment of asthma.

LECTURE NOTES

The material covered by this chapter will easily take up two lectures, and possibly a third. While there is a fair amount of material, most students do not find the concepts, especially the earlier ones, particularly challenging. The structures and chemical nature of lipids should be the subject of a first lecture, leading to the basis of bilayer formation. Membrane structure and function will take at least one lecture as well. Membrane transport and the function of receptor proteins may require a third lecture period.

LECTURE OUTLINE

I. Lipid structures
   A. Fatty acids
      1. Amphipathic nature
      2. Consequences of unsaturation
   B. Triacylglycerols
   C. Phosphoacylglycerols
      1. Phosphatidic acids
      2. Hydrophilic head groups

D. Waxes
E. Sphingolipids
F. Glycolipids
G. Steroids

II. Biological membranes
 A. Lipid bilayers
  1. Importance of hydrophobic interactions
  2. Dissimilarity of outer and inner layers
  3. Fluidity of membranes – contributing factors, importance
  4. Lateral and transverse diffusion in a membrane
 B. Membrane proteins
  1. Integral and peripheral proteins
  2. Transport proteins, membrane-bound enzymes, and receptors
 C. The fluid mosaic model

III. Membrane transport
 A. Passive transport
  1. simple diffusion
  2. facilitated diffusion
 B. Active transport
  1. Primary active transport
  2. Secondary active transport
 C. Membrane receptors

IV. Lipid-soluble vitamins
 A. Vitamin A
 B. Vitamin D
 C. Vitamin E
 D. Vitamin K

V. Prostaglandins and leukotrienes

ANSWERS TO PROBLEMS

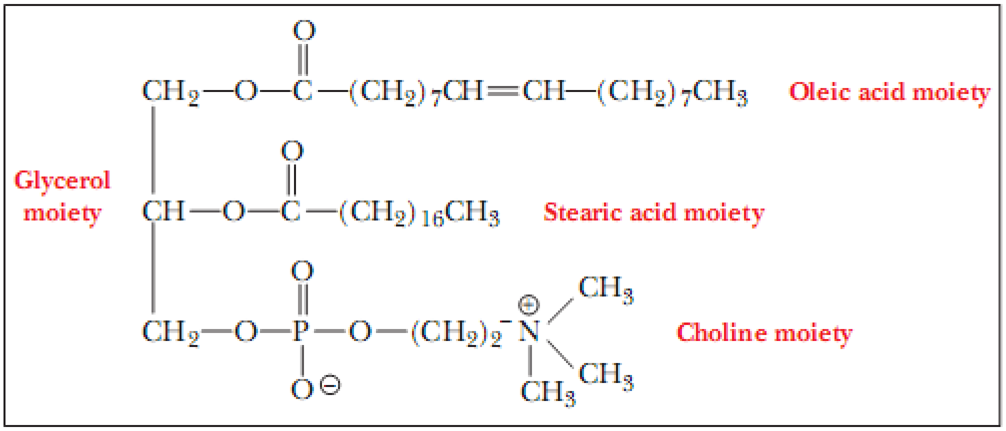
8.1 The Definition of a Lipid

1. Solubility properties (insoluble in aqueous or polar solvents, soluble in nonpolar solvents). Some lipids are not at all structurally related.

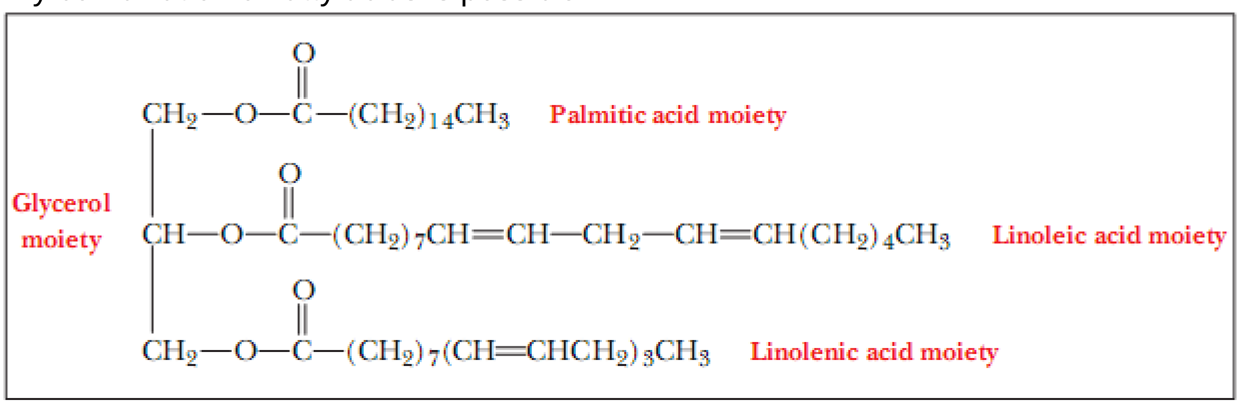
8.2 The Chemical Natures of the Lipid Types

2. In both types of lipids, glycerol is esterified to carboxylic acids, with three such ester linkages formed in triacylglycerols and two in phosphatidyl ethanolamines. The structural difference comes in the nature of the third ester linkage to glycerol. In phosphatidyl ethanolamines, the third hydroxyl group of glycerol is esterified not to a carboxylic acid but to phosphoric acid. The phosphoric acid moiety is esterified in turn to ethanolamine. (See Figures 8.2 and 8.5.)

3.

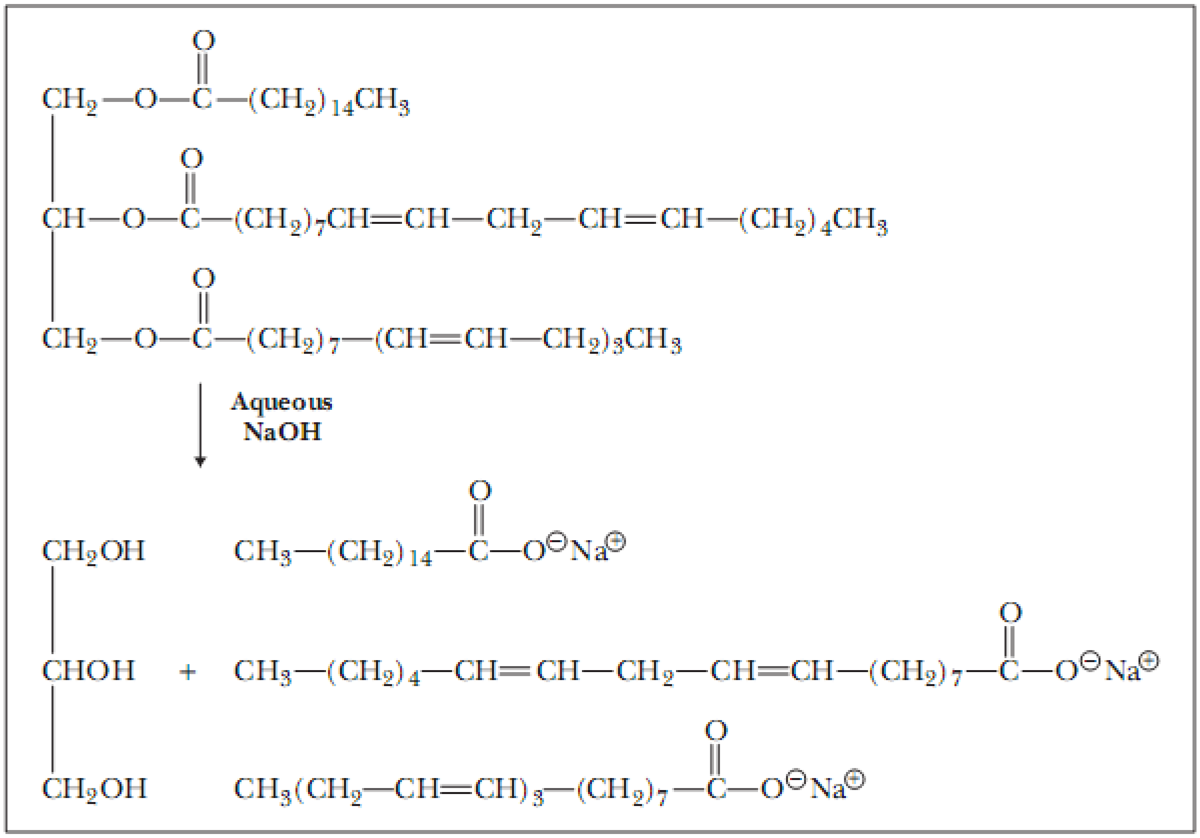


4. Both sphingomyelins and phosphatidylcholines contain phosphoric acid esterified to an amino alcohol, which must be choline in the case of a phosphatidylcholine and may be choline in the case of a sphingomyelin. They differ in the second alcohol to which phosphoric acid is esterified. In phosphatidylcholines, the second alcohol is glycerol, which has also formed ester bonds to two carboxylic acids. In sphingomyelins, the second alcohol is another amino alcohol, sphingosine, which has formed an amide bond to a fatty acid. (See Figure 8.6.)
5. This lipid is a ceramide, which is one kind of sphingolipid.
6. Sphingolipids contain amide bonds, as do proteins. Both can have hydrophobic and hydrophilic parts, and both can occur in cell membranes, but their functions are different.
7. Any combination of fatty acids is possible.



8. Steroids contain a characteristic fused-ring structure, which other lipids do not.
9. Waxes are esters of long-chain carboxylic acids and long-chain alcohols. They tend to be found as protective coatings.
10. Phospholipids are more hydrophilic than cholesterol. The phosphate group is charged, and the attached alcohol is charged or polar. These groups interact readily with water. Cholesterol has only a single polar group, an -OH.

11.



12. The waxy surface coating is a barrier that prevents loss of water.
13. The surface wax keeps produce fresh by preventing loss of water.
14. Cholesterol is not very water-soluble, but lecithin is a good natural detergent, which is actually part of lipoproteins that transport the less soluble fats through the blood.
15. The lecithin in the egg yolks serves as an emulsifying agent by forming closed vesicles. The lipids in the butter (frequently triacylglycerols) are retained in the vesicles and do not form a separate phase.
16. The removal of the oil also removes the natural oils and waxes on the feathers. These oils and waxes must regenerate before the birds can be released.

8.3 Biological Membranes

17. Triacylglycerols are not found in animal membranes.
18. Statements (c) and (d) are consistent with what is known about membranes. Covalent bonding between lipids and proteins [statement (e)] occurs in some anchoring motifs, but is not widespread otherwise. Proteins “float” in the lipid bilayers rather than being sandwiched between them [statement (a)]. Bulkier molecules tend to be found in the outer lipid layer [statement (b)].
19. The public is attuned to the idea of polyunsaturated fats as healthful. The *trans* configuration gives a more palatable consistency. Recently, however, concerns have arisen about the extent to which such products mimic saturated fats.

20. Partially hydrogenated vegetable oils have the desired consistency for many foods, such as oleomargarine and components of TV dinners.
21. Many of the double bonds have been saturated. Crisco contains “partially hydrogenated vegetable oils.”
22. Less heart disease is associated with diets low in saturated fatty acids.
23. The transition temperature is lower in a lipid bilayer with mostly unsaturated fatty acids compared with one with a high percentage of saturated fatty acids. The bilayer with the unsaturated fatty acids is already more disordered than the one with a high percentage of saturated fatty acids.
24. Myelin is a multilayer sheath consisting mainly of lipids (with some proteins) that insulates the axons of nerve cells, facilitating transmission of nerve impulses.
25. At the lower temperature, the membrane would tend to be less fluid. The presence of more unsaturated fatty acids would tend to compensate by increasing the fluidity of the membrane compared to one at the same temperature with a higher proportion of saturated fatty acids.
26. The higher percentage of unsaturated fatty acids in membranes in cold climates is an aid to membrane fluidity.
27. Hydrophobic interactions among the hydrocarbon tails are the main energetic driving force in the formation of lipid bilayers.
28. The relative amounts of cholesterol and phosphatidylcholine can vary widely in different types of membranes in the same cell (see Table 8.3).

8.4 The Kinds of Membrane Proteins

29. Lipids can be “tagged” with a fluorescent moiety to observe their motion in membranes. Proteins have intrinsic fluorescence and can be monitored directly.
30. A glycoprotein is formed by covalent bonding between a carbohydrate and a protein, whereas a glycolipid is formed by covalent bonding between a carbohydrate and a lipid.
31. Proteins that are associated with membranes do not have to span the membrane. Some can be partially embedded in it, and some associate with the membrane by noncovalent interactions with its exterior.
32. A 100-g sample of membrane contains 50 g of protein and 50 g of phosphoglycerides.

$$50 \text{ g lipid} \times \frac{1 \text{ mol lipid}}{800 \text{ g lipid}} = 0.0625 \text{ mol lipid}$$

$$50 \text{ g protein} \times \frac{1 \text{ mol protein}}{50{,}000 \text{ g protein}} = 0.001 \text{ mol protein}$$

The molar ratio of lipid to protein is 0.0625/0.001 or 62.5/1.
33. Nature chooses what works. This is an efficient use of a large protein and of the energy of ATP.
34. In a protein that spans a membrane, the nonpolar residues are the exterior ones; they interact with the lipids of the cell membrane. The polar residues are in the interior, lining the channel through which the ions enter and leave the cell.

8.5 The Fluid-Mosaic Model of Membrane Structure

35. Statements (c) and (d) are correct. Transverse diffusion is only rarely observed [statement (b)], and the term *mosaic* refers to the pattern of distribution of proteins in the lipid bilayer [statement (e)]. Peripheral proteins are also considered part of the membrane [statement (a)].
36. Phosphorylation of tyrosine residues can activate or deactivate a receptor protein, depending on the specific system.
37. The action of a number of receptor proteins requires binding of GTP to a specific subunit, followed by subsequent hydrolysis.

8.6 The Functions of Membranes

38. Biological membranes are highly nonpolar environments. Charged ions tend to be excluded from such environments rather than dissolving in them, as they would have to do to pass through the membrane by simple diffusion.
39. Statements (a) and (c) are correct; statement (b) is not correct because ions and larger molecules, especially polar ones, require channel proteins.

8.7 Lipid-Soluble Vitamins and Their Functions

40. Cholesterol is a precursor of vitamin D_3; the conversion reaction involves ring opening.
41. Vitamin E is an antioxidant.
42. Isoprene units are five-carbon moieties that play a role in the structure of a number of natural products, including fat-soluble vitamins.
43. See Table 8.4.
44. The *cis–trans* isomerization of retinal in rhodopsin triggers the transmission of an impulse to the optic nerve and is the primary photochemical event in vision.
45. Vitamin D can be made in the body.
46. Lipid-soluble vitamins accumulate in fatty tissue, leading to toxic effects. Water-soluble vitamins are excreted, drastically reducing the chances of an overdose.
47. Vitamin K plays a role in the blood-clotting process. Blocking its mode of action can have an anticoagulant effect.
48. Vitamins A and E are known to scavenge free radicals, which can do oxidative damage to cells.
49. Eating carrots is good for both. Vitamin A, which is abundant in carrots, plays a role in vision. Diets that include generous amounts of vegetables are associated with a lower incidence of cancer.

8.8 Prostaglandins and Leukotrienes

50. An omega-3 fatty acid has a double bond at the third carbon from the methyl end.
51. Leukotrienes are carboxylic acids with three conjugated double bonds.
52. Prostaglandins are carboxylic acids that include a five-membered ring in their structure.
53. Prostaglandins and leukotrienes are derived from arachidonic acid. They play a role in inflammation and in allergy and asthma attacks.
54. Prostaglandins in blood platelets can inhibit their aggregation. This is one of the important physiological effects of prostaglandins.